

61. The method of claim 1, wherein the isostabilizing agent is TMAC, and wherein the nucleic acid molecule is poly(dT) and is linked to a non-reacting structure, and further comprising c) washing the poly(dT) nucleic acid molecule with a wash solution comprising a salt.--

## II. RESPONSE

In response to the restriction requirement which the Examiner imposed, Applicant elects, with traverse, to prosecute claims 1-30 and 60, *i.e.*, the Group I claims.

As discussed in the telephone conference with Examiner Katcheves on November 1, 2002, which Applicant's representative sincerely appreciates, Applicant proposes that the claims of Groups I and II be rejoined. Both groups are directed to methods for purifying poly(A) RNA from a sample and kits for use therefor. Claim 1, which is representative of the Group I method claims, recites a) incubating a sample with a nucleic acid and b) isolating the nucleic acid molecule. Claim 31, which is representative Group II method claims, generally recites those steps and further recites that the nucleic acid is washed. The washing step is included in claim 13, which is dependent from claim 1. Therefore, the steps of the claims are similar and overlapping.

One difference discernable between claim 1 of the Group I claims and claim 31 of the Group II claims is the recitation of a non-reacting structure in claim 31. Applicant notes that claim 18, which is dependent from claim 1, recites a non-reacting structure. A search done with respect to the method of claim 31 will generally address the patentability of claim 1 from a prior art standpoint because of the overlap in the elements and steps of the claims. Thus, it would not be a serious burden on the examiner to do a search that would cover both groups of claims. Applicant respectfully requests that the restriction of the claims be withdrawn.



Applicant also wishes to add a claim to this case, which emphasizes the argument above.

Claim 61 is added as a dependent claim from claim 1, with similar limitations as claim 31. No new matter is being added based on the claims originally filed in this case. A copy of the pending claims, should the Examiner rejoin the groups, is provided for the Examiner's convenience in Appendix A.

Applicant's representative thanks the Examiner for her time on the telephone conference and consideration of the above arguments. The Examiner is invited to contact the undersigned attorney at (512) 536-3081 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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## APPENDIX: A

### Pending Claims as of Response to Restriction Requirement Dated October 1, 2002

1. A method for purifying poly(A) RNA from a sample comprising:
  - a) incubating a composition comprising:
    - i) the sample;
    - ii) a poly(dT) or poly(U) nucleic acid molecule; and
    - iii) an isostabilizing agent, wherein the isostabilizing agent is tetramethylammonium chloride (TMAC) or tetraethylammonium chloride (TEAC),  
under conditions allowing poly(A) RNA to hybridize with the poly(T) nucleic acid molecule; and
  - b) isolating the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) RNA.
2. The method of claim 1, wherein the final concentration of the isostabilizing agent in the composition is between about 1.0 M and about 3.0 M.
3. The method of claim 2, wherein the final concentration of the isostabilizing agent in the composition is between about 1.2 M and about 2.4 M.
4. The method of claim 3, wherein the final concentration of the isostabilizing agent in the composition is between about 1.5 M and about 2.0 M.
5. The method of claim 1, wherein the isostabilizing agent is provided to the composition in a hybridization solution.
6. The method of claim 1, wherein the composition further comprises CHAPS in a final concentration between about 0.5% and about 2.0%.

7. The method of claim 1, wherein the composition further comprises Triton X-100.
8. The method of claim 7, wherein the concentration of Triton X-100 in the composition is between about 0.01% and about 0.1%.
9. The method of claim 5, wherein the hybridization solution further comprises Triton X-100.
10. The method of claim 1, further comprising heating the composition at a temperature between about 70°C and about 90°C prior to incubation under hybridization conditions.
11. The method of claim 1, wherein the hybridization conditions comprise incubating the composition between about 15°C and 50°C for at least 10 minutes to 48 hours.
12. The method of claim 11, wherein the incubation time is at least 4 hours.
13. The method of claim 1, further comprising washing the poly(T) or poly(U) nucleic acid molecule and the hybridized poly(A) RNA in wash solution comprising an isostabilizing agent.
14. The method of claim 13, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) RNA are washed more than once.
15. The method of claim 13, wherein the isostabilizing agent is TMAC or TEAC.
16. The method of claim 15, wherein the concentration of the isostabilizing agent in the wash solution is between about 0.05 M and about 3.0 M.
17. The method of claim 14, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) RNA are washed at least once in a wash solution with an isostabilizing agent



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concentration greater than about 1.2 M and at least once in a wash solution with an isostabilizing agent concentration of less than about 0.5 M.

18. The method of claim 1, wherein the poly(dT) or poly(U) nucleic acid molecule is linked to a non-reacting structure.

19. The method of claim 18, wherein the non-reacting structure is cellulose.

20. The method of claim 18, further comprising isolating the non-reacting structure linked to the oligonucleotide that is hybridized to poly(A) RNA.

21. The method of claim 20, further comprising washing the non-reacting structure.

22. The method of claim 18, wherein the non-reacting structure is a bead.

23. The method of claim 22, wherein the bead is magnetic.

24. The method of claim 23, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) RNA are isolated from the sample with a magnet.

25. The method of claim 20, wherein the non-reacting structure is isolated from the sample by centrifugation or filtration.

26. The method of claim 18, further comprising eluting the poly(A) RNA from the non-reacting structure with an eluting solution of low ionic strength.

27. The method of claim 26, wherein the eluting solution comprises sodium citrate.

28. The method of claim 1, wherein the poly(dT) or poly(U) nucleic acid molecule is biotinylated.



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29. The method of claim 28, further comprising
  - c) incubating the biotinylated oligonucleotide and the sample with avidin or streptavidin linked to a non-reacting structure; and
  - d) eluting the poly(A) RNA from the non-reacting structure with an eluting solution.
30. The method of claim 1, wherein the sample or the hybridization solution does not contain guanidinium.
31. A method for purifying poly(A) RNA from a sample comprising:
  - a) incubating the sample with a poly(dT) oligonucleotide connected to a non-reacting structure and a hybridization solution comprising tetramethylammonium under conditions allowing poly(A) RNA to hybridize with the oligonucleotide;
  - b) isolating the oligonucleotide with the hybridized poly(A) RNA away from the sample; and
  - c) washing the oligonucleotide with a wash solution comprising a salt.
32. The method of claim 31, wherein the non-reacting structure is cellulose.
33. The method of claim 31, wherein the oligonucleotide is biotinylated.
34. The method of claim 33, further comprising
  - c) incubating the biotinylated oligonucleotide and the sample with avidin or streptavidin linked to a non-reacting structure; and
  - d) eluting the poly(A) RNA from the non-reacting structure with an eluting solution.
35. The method of claim 34, further comprising isolating the non-reacting structure linked to the oligonucleotide hybridized to poly(A) RNA by centrifugation or filtration.

36. The method of claim 31, further comprising eluting the poly(A) RNA from the non-reacting structure with an eluting solution with low ionic strength.
37. A kit, in a suitable container means, comprising:
- a) a poly(dT) oligonucleotide linked to a non-reacting structure; and
  - b) binding solution comprising an isostabilizing agent.
38. The kit of claim 37, wherein the isostabilizing agent in the binding solution is TMAC or TEAC.
39. The kit of claim 38, wherein the concentration of TMAC or TEAC in the binding solution is between about 1.0 M and about 5.0 M.
40. The kit of claim 39, wherein the concentration of TMAC or TEAC in the binding solution is about 4.0 M.
41. The kit of claim 39, wherein the concentration of TMAC or TEAC in the binding solution is about 2.0 M.
42. The kit of claim 37, wherein the binding solution further comprises at least one detergent.
43. The kit of claim 42, wherein the detergent is Triton X-100 or CHAPS, or a combination of Triton X-100 and CHAPS.
44. The kit of claim 43, wherein the concentration of the detergent in the binding solution is between about 0.001% to about 1.0%.
45. The kit of claim 37, further comprising a detergent in a concentration of between about 0.01% and 0.1%.

46. The kit of claim 37, further comprising a wash solution comprising an isostabilizing agent.
47. The kit of claim 46, wherein the isostabilizing agent in the wash solution is TMAC or TEAC.
48. The kit of claim 47, wherein the concentration of TMAC or TEAC in the wash solution is between about 0.1 M and about 2.0 M.
49. The kit of claim 48, wherein the concentration of TMAC or TEAC in the wash solution is about 2.0 M.
50. The kit of claim 37, further comprising an elution solution of low ionic strength comprising a chelating salt.
51. The kit of claim 50, wherein the salt in the elution solution is sodium citrate or EDTA-2Na.
52. The kit of claim 50, wherein the concentration of the salt in the elution solution is between about 0.1 mM and about 100 mM.
53. The kit of claim 37, wherein the oligonucleotide is biotinylated.
54. The kit of claim 53, wherein the non-reacting structure is a streptavidin or avidin matrix.
55. The kit of claim 37, wherein the non-reacting structure is cellulose.
56. The kit of claim 37, wherein the non-reacting structure is a bead.
57. The kit of claim 56, wherein the bead is magnetic.





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58. The kit of claim 57, further comprising a magnetic stand.
59. The kit of claim 37, further comprising a filtration device.
60. A kit, in suitable container means, comprising:
- a) a poly(dT) oligonucleotide linked to cellulose;
  - b) hybridization solution comprising tetramethylammonium (TMAC) in a concentration of between about 1.2 M and about 4 M and Triton X-100 in a concentration of between about 0.03% and about 0.1%;
  - c) a first wash solution comprising TMAC in a concentration of about 2 M;
  - d) a second wash solution comprising TMAC in a concentration of about 0.4 M; and
  - e) elution solution having a total ionic strength of less than 0.01.
61. The method of claim 1, wherein the isostabilizing agent is TMAC, and wherein the nucleic acid molecule is poly(dT) and is linked to a non-reacting structure, and further comprising c) washing the poly(dT) nucleic acid molecule with a wash solution comprising a salt.